

LISTING OF THE CLAIMS

Claim 1 (canceled)

Claim 2 (currently amended) A method according to ~~claim 1~~ for the production of a single heavy chain antibody in a non-human mammal comprising expressing a heterologous VHH heavy chain locus in that mammal specifically in B cells in response to antigen challenge wherein the VHH heavy chain locus comprises:

(a) ~~at least one VHH region each comprising one VHH exon, at least one D region each comprising one D exon and at least one J region each comprising one J exon,~~ wherein the VHH exon region, the D exon region and the J exon region are capable of recombining to form VDJ coding sequence,

(b) a constant heavy chain region comprising at least one constant heavy chain gene, wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain,

(c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells and

~~which locus when expressed leads to the formation of a single heavy chain antibody~~
said method comprising:

- 1) immunizing said mammal with an antigen and
- 2) isolating single heavy chain antibody against said antigen from said mammal.

Claim 3 (canceled)

Claim 4 (currently amended) A method according to ~~claim 3~~ for the production of

a single heavy chain antibody in a non-human mammal comprising expressing a camelised VH heavy chain locus in that mammal specifically in B cells in response to antigen challenge wherein the camelised VH heavy chain locus comprises:

(a) ~~at least one VH-region-each-comprising-one~~ VH exon which is mutated such that, when expressed, the resulting single heavy chain antibody is stabilised, at least one ~~D region-each-comprising-one~~ D exon and at least one ~~J-region-comprising-one~~ J exon, wherein the VH exonregion, the D exonregion and the J exonregion are capable of recombining to form VDJ coding sequence, and

(b) a constant heavy chain region comprising at least one constant heavy chain gene, wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain,

(c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells

~~and which locus when expressed leads to the formation of a single heavy chain antibody~~
said method comprising:

1) immunizing said mammal with an antigen and

2) isolating single heavy chain antibody against said antigen from said mammal.

Claims 5 – 6 (canceled)

Claim 7 (currently amended) A method according to claim 1-~~or~~ 2 wherein the VHH single heavy chain locus comprises a camelid VHH, at least one D exonregion of human origin and at least one J exonregion of human origin and a constant region of human origin.

Claim 8 (**currently amended**) A method according to claim ~~3~~ 4 wherein the camelised VH heavy chain locus comprises at least one D ~~exon~~region of human origin and at least one J ~~exon~~region of human origin and a constant region of human origin.

Claim 9 (**canceled**)

Claim 10 (**currently amended**) A method according to claim ~~1~~ ~~or~~ ~~3~~ 2 or 4 wherein the constant heavy chain region comprises at least one constant region heavy chain gene which is of non-camelid origin.

Claim 11 (**original**) A method according to claim 10 wherein at least one constant region heavy chain gene is of human origin.

Claims 12 – 16 (**canceled**)

Claims 17 - 32 (**canceled**)

Claim 33 (**currently amended**) The method of claim ~~1~~ ~~or~~ 2 wherein the entire VHH single heavy chain locus is of camelid origin

Claim 34 (**currently amended**) The method of claim ~~3~~ ~~or~~ 4 wherein the camelised VH single heavy chain locus is of human origin.

Claim 35 (**currently amended**) The method of claim ~~3~~ ~~or~~ 4 wherein the camelised VH single heavy chain locus is of non-human origin.

Claim 36 (**currently amended**) The method of claim ~~3~~ ~~or~~ 4 wherein the camelised VH single heavy chain locus is of camelid origin.

Claims 37-38 (**canceled**)

Claim 39 (**new**) The method according to claim 2 or 4 wherein the non-human

DOCKET NO.: CARP0015-100

PATENT

APPLICATION SERIAL NO. 10/693,308

RESPONSE TO FINAL REJECTION DATED FEBRUARY 12, 2007

mammal is a rodent.

Claim 40 (**new**) The method according to claim 2 or 4 wherein the regulatory sequence is a locus control region.